

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Martha G. Welch et al.	Confirmation No.:	8041
Application No.:	10/799,941	Art Unit:	1654
Filed:	March 11, 2004	Examiner:	Andrew D. Kosar
Title:	NOVEL MULTIPEPTIDE REGIMEN FOR THE TREATMENT OF AUTISTIC SPECTRUM, BEHAVIORAL, EMOTIONAL AND VISCERAL INFLAMMATION/AUTOIMMUNE DISORDERS		

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. §1.131

We, Martha G. Welch, David A. Ruggiero, and Muhammad Anwar, hereby declare as follows:

1. We are co-inventors of the subject matter claimed in the patent application having U. S. Serial No. 10/799,941.
2. We have been informed that the claims now pending in this application are directed to a pharmaceutical composition comprising a therapeutically effective amount of secretin in combination with a therapeutically effective amount of oxytocin.
3. We have been informed that pending claims of the '941 application have been rejected by the patent Examiner over Hollander (U.S. Pub. No. 2006/0105939) in view of an on-line NIH news alert ("The Use of Secretin to Treat Autism" Internet document), and further in view of Swain (E. Swain, Pharmaceutical and Medical Packaging News) and PIERCE (PIERCE Technical Resource Sheet TR0043.0 "Protein Stability and Storage").
4. We conceived of the pharmaceutical composition claimed in the '941 application at least prior to August 17, 2001 as evidenced by the experiments and notes included in the laboratory notebooks attached. A redacted copy of relevant lab notebook entries is attached as **Exhibit A**.
5. We diligently reduced the claimed invention to practice.
6. The claimed invention was conceived and reduced to practice in the United States.

7. The work described within this Declaration was performed by us, or on our behalf under our supervision.

8. We hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the patent in which this declaration is made.

Date: _____

Martha G. Welch

Date: 9-18-08 _____

David A. Ruggiero

David A. Ruggiero

Date: _____

Muhammad Anwar

7. The work described within this Declaration was performed by us, or on our behalf under our supervision.

8. We hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the patent in which this declaration is made.

Date:

9/16/08


Martha G. Welch

Date:

David A. Ruggiero

Date:

9-16-08

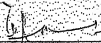

Muhammad Anwar

EXHIBIT A

SECRETIN

S-1

Animal wt 250-275 g cannulated 4 days before exp.
 lateral v AP 7.1 mm 1.1.8 D-3 (Cx)
 Secretin 10 μ g/10 μ l in PB a.i.m.
 control 10 μ l PB a.i.m.
 Both injections \rightarrow total all at once slowly
 waited 3 hrs
 Perfused 4% PFA
 overnight 10% sucrose
 CFS + Nissl.

control animal processed (same wt) on

S-2

Animal wt 250-275 g cannulated 4 days before exp.
 as above
 Secretin (5 μ g/5 μ l X3) at 15 min intervals
 PB (cont) (5 μ l X3) " " "
 waited 3 hrs
 Perfused 4% PFA
 CFS + Nissl.

S-3

Anti Secretin Ab Tests.

11/00/00

2 slides.

SECRETIN

S-4

calcium

(Rat wt 275 g)

5g in 10 ml saline
 injected slowly
 survival 24 hrs
 Perfusion 4% PFA

X Secretin 1:5000

6 slides

S-5

calcium

(Rat wt 275 g)

5g in 10 ml saline
 injected
 as above

oxy 1:5000

Secretin 1:5000

Double/ Secretin DAB oxy Gold

control 1:5000 normal Rabbit Serum

S-6

Rat wt 455g (6 month old)

accumulated 4 days before injection
 Secretin 5mg / 5 ml PB a.i.v. x 3 interval 15 min
 waited 3 hrs before perfusion

Perfused 4% PFA

Day 1

CFOS 1:8000

(to be stained for Nissl)

Double

CFOS / oxy 1:5000

CFOS / Secretin 1:5000

CFOS / SHF 1:10000

used Biotin/ABC for CFOS

used Peroxidase

conjugated by

4% formal

oxy. Sec. + SHF

SECRETIN

S-7 (Rate 250/75g) cannulated 5 days before injection

AP = 17.0 mm

L = 1.8 mm

D = 3.0 mm (from SA)

Double Dose

Secretin 10ug/5ul x3 (5 min interval)

CONTROL (no injection)

waited 2 hrs

Perfusion 4% PFA overnight fix

Both animal entire brain to Frontal ex 2nd
 T. spinal cord
 Adrenal
 Pituitary & Pinal

Posterior fix

CFS - Nissl

CFS - Oxy

CFS - Secretin } limited to PVN area

CFS - CRH }

DATE

TOPIC: SHR /WKY

TS-13

Refused

Picked

SHRWKY

Hedulla

CFos/Nissl

CFos/Nissl

CFos/PNMT

CFos/PNMT

CFos/R1

CFos/R1

Fore Brain

CFos/Nissl

CFos/Nissl

CFos/R1

CFos/R1

CFos/TH

CFos/TH

CFos/Secretin

CFos/Secretin

T1

CFos/TH

CFos/TH

DATE: _____

TOPIC: _____

CP-52 (CONT)

(Perfused)

sagittal 16 μ

minuted Saline Pump = 21.72g

minuted cocaine 30.31g

Post fixed overnight with 3% PFA in 10% sucrose
cut on cryostat sagittal

(Perfused)

4% PFA

overnight 10% sucrose

Saline 39.50g

cocaine 49.05g

cut coronal 30 μ

order of collection & Processing

① Apoptotic

④ TH

② c-Fos

⑤ PMMT

③ GABA

⑥ Succin

⑦ oxy/cocaine

Adrenal gland

c-Fos

c-Fos/TH

c-Fos/PMAT

Heart

Frozen for c-Fos/Apopt / TH

DATE

TOPIC: Secretin/Oxy

CP-53

P-13 mother arrived on the
Plug

ONE DAY OLD (Exp) stressed by separation 3 min
Reunited 15 min
Separated 3 min
Reunited 15 min
Separated 3 min
Reunited 2 1/2 hrs

(CONT) NO separation

Sagittal Sections Thru Pituitary & Pituitary glands
also Pancreas.

CPDS/TH Secretin oxy

4 DAYS OLD

in one pair Repeated the above procedure,

in second pair one baby separated for longer (14 days)
survived

12 DAYS OLD

Repeated the above procedure
Day One procedure

14/20 days old

Both previously (11th day) stressed
and a new baby stressed
according to Pearson method and
prepared for Sec. Oxy, CFS.

DATE: _____

TOPIC: Piglet (Secretin) _____

CP-59 / ~~P666~~ (only for Secretin) & lat. ~~signatures~~

6 days old ♂

Perfused 4% PFA (3 lit)

30 μ l Sections (FR Sagittal Medull Coronal)

PNMT 1:15000 (Medulla)

CART 1:10000 (Medulla, FR)

Sec 1:5000 (chemico FR)

Sec 1:10000 (Plexus FR)

oxy 1:10000 (chemico FR)

DATE:

TOPIC: Hypoxia

CP-60/PG-19

2 Piglet (10 days old)

performed on

Medulla Processed for

fos / TH

fos / POMT

fos / TH

fos / SST

Tomy, Sica

PG-19

Fore Brain

Double label for

fos / Secretin

fos / oxytocin

DATE:

TOPIC: IBD

CP-63

6 Rat Gut approximately 225 received on

4	for IBD]
2	" CONT	

TWBS Dose

Day 1 Cont Cont Dose

Oxy 242 ml

Day 3

Oxy 242 ml

Day 8

AL2A Punks on

Animal	1.	CONT	no treatment
	2.	CONT	Oxy + Sec
"	3.	IBD	Oxy + Sec
"	4.	IBD	Oxy
"	5.	IBD	Sec
"	6.	Did not	

Survived 5 days

Perfusion 19/6 w.d.

C. coli, L. acid

CONT

IBD

IBD 200 ml
 CONT 200 ml

Pec - 200 ml

TWBS - 200 ml

Oxy 242 ml

IBD 200 ml - 1 ml

1000 ml

DATE:

TOPIC: 186

CP-64

8 Rat IBD wt 250g

4 CONT

1 TNBS

one cont did

TNBS

Doses

Double as of CP-63

oxy 0.84/100 ml

Sec 0.84

DATE

TOPIC: Sec/Oxy Collection

CP-65

Sec

2 Nov 2.5 pt Collection (15 mg / 1 ml Saline)
Survived overnight

Rats died